

In the Claims

1-55 (canceled).

56 (new). A composition of matter comprising:

a) an isolated antibody, monoclonal antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors;

b) an isolated antibody, monoclonal antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors and said antibody binds KIR2DL1 and KIR2DL2/3;

c) an isolated antibody, monoclonal antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors, said antibody binds KIR2DL1 and KIR2DL2/3 and wherein said antibody inhibits the binding of a HLA-C allele molecule having a Lys residue at position 80 to a human KIR2DL1 receptor and the binding of a HLA-C allele molecule having an Asn residue at position 80 to human KIR2DL2/3 receptors;

d) an isolated antibody, monoclonal antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors, said antibody binds KIR2DL1 and KIR2DL2/3, said antibody inhibits the binding of a HLA-C allele molecule having a Lys residue at position 80 to a human KIR2DL1 receptor and the binding of a HLA-C allele molecule having an

Asn residue at position 80 to human KIR2DL2/3 receptors, and said antibody binds to substantially the same epitope as monoclonal antibody DF200;

e) a pharmaceutically acceptable carrier or excipient and an isolated antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on NK cells expressing at least one of said two different human inhibitory KIR receptors, said antibody being present in an amount effective to detectably potentiate NK cell cytotoxicity in a patient or in a biological sample comprising NK cells;

f) a pharmaceutically acceptable carrier or excipient; a therapeutic agent selected from an immunomodulatory agent, a hormonal agent, a chemotherapeutic agent, an anti-angiogenic agent, an apoptotic agent, a second antibody that binds to and inhibits an inhibitory KIR receptor, an anti-infective agent, a targeting agent or an adjunct compound; and an isolated antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on NK cells expressing at least one of said two different human inhibitory KIR receptors, said antibody being present in an amount effective to detectably potentiate NK cell cytotoxicity in a patient or in a biological sample comprising NK cells;

g) a hybridoma comprising a B cell from a non-human mammalian host that has been immunized with an antigen that comprises an epitope present on an inhibitory KIR polypeptide, fused to an immortalized cell, wherein said hybridoma produces a monoclonal antibody that binds at least two different human inhibitory KIR receptor gene products and is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products;

h) a hybridoma comprising a B cell from a non-human mammalian host that has been immunized with an antigen that comprises an epitope present on an inhibitory KIR polypeptide, fused to an immortalized cell, wherein said hybridoma produces a monoclonal antibody that binds at least two different human inhibitory KIR receptor gene products and is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two

different human inhibitory KIR receptor gene products and said hybridoma does not produce monoclonal antibody NKVSF1;

i) a hybridoma comprising a B cell from a non-human mammalian host that has been immunized with an antigen that comprises an epitope present on an inhibitory KIR polypeptide, fused to an immortalized cell, wherein said hybridoma produces a monoclonal antibody that binds at least two different human inhibitory KIR receptor gene products and is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products and said antibody binds KIR2DL1 and KIR2DL2/3;

j) a hybridoma comprising a B cell from a non-human mammalian host that has been immunized with an antigen that comprises an epitope present on an inhibitory KIR polypeptide, fused to an immortalized cell, wherein said hybridoma produces a monoclonal antibody that binds at least two different human inhibitory KIR receptor gene products and is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products, said antibody binds KIR2DL1 and KIR2DL2/3 and said hybridoma produces an antibody that inhibits the binding of a HLA-c allele molecule having a Lys residue at position 80 to a human KIR2DL1 receptor and the binding of a HLA-C allele molecule having an Asn residue at position 80 to human KIR2DL2/3 receptors;

k) a hybridoma comprising a B cell from a non-human mammalian host that has been immunized with an antigen that comprises an epitope present on an inhibitory KIR polypeptide, fused to an immortalized cell, wherein said hybridoma produces a monoclonal antibody that binds at least two different human inhibitory KIR receptor gene products and is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products, said antibody binds KIR2DL1 and KIR2DL2/3 and said hybridoma produces an antibody that binds to substantially the same epitope as monoclonal antibody DF200 produced by hybridoma DF200; or

l) the hybridoma identified as DF200.

57 (new). The antibody of claim 56, wherein said antibody is a monoclonal antibody or a fragment of a monoclonal antibody.

58 (new). The antibody of claim 56, wherein said antibody is monoclonal antibody DF200 or a fragment thereof.

59 (new). The antibody of claim 56, further comprising a conjugated or covalently bound toxin, detectable moiety, or solid support.

60 (new). A method of producing an antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products, said method comprising the steps of:

- a) selecting, from a library or repertoire of antibodies, an antibody or an antibody fragment that cross-reacts with at least two different human inhibitory KIR2DL receptor gene products, and
- b) selecting an antibody of (a) that capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on a population of NK cells expressing said at least two different human inhibitory KIR2DL receptor gene products.

61 (new). The method according to claim 60, wherein said method comprises the immunization of a non-human animal with an inhibitory KIR polypeptide to generate said library or repertoire of antibodies.

62 (new). The method according to claim 60, wherein said antibody is monoclonal.

63 (new). The method according to claim 62, further comprising isolating DNA encoding said antibody; optionally, modifying said DNA to encode a modified or derivatized

antibody selected from a humanized antibody, a chimeric antibody, a single chain antibody or an immunoreactive fragment thereof and transfecting a cell with said DNA.

64 (new). The method according to claim 63, wherein said method further comprises culturing said cell under conditions that allow for the expression of the antibody encoded by said DNA.

65 (new). The method according to claim 64, further comprising isolating the expressed antibody.

66 (new). A method of potentiating NK cell activity in a patient in need thereof, comprising the step of administering to said patient a composition comprising a pharmaceutically acceptable carrier or excipient and an antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity on NK cells expressing at least one of said two different human inhibitory KIR receptors, said antibody being present in an amount effective to detectably potentiate NK cell cytotoxicity in a patient or in a biological sample comprising NK cells.

67 (new). The method of claim 66, wherein said patient is suffering from cancer, another proliferative disorder, an infectious disease or an immune disorder.

68 (new). A method of detecting the presence of NK cells bearing an inhibitory KIR on their cell surface in a biological sample or a living organism, said method comprising the steps of:

a) contacting said biological sample or living organism with an antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors, wherein said antibody, monoclonal antibody, humanized antibody or chimeric antibody is conjugated or covalently bound to a detectable moiety; and

- b) detecting the presence of said antibody in said biological sample or living organism.

69 (new). A method of purifying from a sample NK cells bearing an inhibitory KIR on their cell surface comprising the steps of:

- a) contacting a sample with an antibody, monoclonal antibody, humanized antibody or chimeric antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in NK cells expressing at least one of said two different human inhibitory KIR receptors under conditions that allow said NK cells bearing an inhibitory KIR on their cell surface to bind to said antibody, wherein said antibody, monoclonal antibody, humanized antibody or chimeric antibody is conjugated or covalently bound to a solid support; and
- b) eluting said bound NK cells from said antibody conjugated or covalently bound to a solid support.